

## REMARKS

### Telephone Interview

Applicants would like to express their appreciation to Examiner Chernyshev for the courtesy extended to Applicants' agent, Angela Dallas Sebor, in the informal telephone interview of November 25, 2003. During the interview, Dr. Sebor proposed to limit the claims to proteins encoded by nucleic acid sequences that are at least 90% identical to a nucleic acid sequence encoding FGF-2. Using the Examiner's calculations, this would result in an amino acid sequence that is no less than 70% identical to FGF-2, which the Examiner has indicated would be supported and enabled by the specification. The Examiner agreed that such an amendment would be likely to address the remaining issues under 35 U.S.C. § 112, first paragraph, and encouraged Applicants to submit such amendments.

### Claim Amendments:

The claims have been amended in a manner discussed with the Examiner on November 25. Specifically, independent Claim 1 has been amended to recite in part (a) that the biologically active fibroblast growth factor-2 (FGF-2) protein has an amino acid sequence that is encoded by a nucleic acid sequence that is at least about 90% identical to a nucleic acid sequence encoding a fibroblast growth factor-2 (FGF-2) protein represented by SEQ ID NO:5 or SEQ ID NO:6. Support for this amendment is in previously entered Claim 44 and in the specification on page 17, lines 11-16.

Claim 12 has been amended to remove redundant subject matter.

Claims 17, and 42-47, have been cancelled, without prejudice to or disclaimer of the subject matter therein.

### Objection to the Specification and Rejection of Claims 1-3, 6, 8, 10-18 and 43-46 Under 35 U.S.C. § 112, First Paragraph:

The Examiner has objected to the specification and rejected Claims 1-3, 6, 8, 10-18 and 43-46 under 35 U.S.C. § 112, first paragraph, on the basis of enablement. Specifically, the Examiner contends that the specification, while being enabling for a chimeric protein comprising a biologically active FGF-2 protein having an amino acid sequence that is at least 70% identical to SEQ ID NO:5 or SEQ ID NO:6, is allegedly not enabling for a chimeric protein comprising a biologically active

FGF-2 protein that is encoded by a nucleic acid sequence that is at least 70% identical to a nucleic acid sequence encoding SEQ ID NO:5 or SEQ ID NO:6. The Examiner explains that the claim as previously presented includes a sequence in which one can change up to 30%[sic] of the nucleic acid sequence and in doing so, can also choose to change only one nucleotide per three-nucleotide codon. Each of SEQ ID NOs:5 and 6 are 146 amino acid sequences (i.e., would be encoded by a nucleotide sequence of 438 nucleotides). If one changed 30% of the 438 nucleotide sequence, one could potentially change up to 131 nucleotides at one nucleotide per codon (i.e., 131 out of 146 codons), which could potentially result in an amino acid sequence that is only ~10% identical to SEQ ID NO:5 or 6.

Applicants have amended Claim 1 to address the Examiner's concerns as discussed above and as discussed with the Examiner on November 25. Specifically, Applicants have amended Claim 1 to recite identity of 90% at the nucleotide level, instead of 70% identity. Using the Examiner's calculation method above, if one changed up to 10% of the nucleotide sequence encoding SEQ ID NO:5 or 6, which is 43.8 out of 438 nucleotides (Applicants will assume 44 nucleotides for the sake of argument), and if one assumes that this could result in a change in up to 44 of the codons in the nucleotide sequence (i.e., a change in 44 out of 146 of the amino acid residues in SEQ ID NO:5 or 6), the resulting protein would be no less than ~70% identical to SEQ ID NO:5 or 6 (i.e.,  $102/146 = \sim 70\%$ ). The Examiner has acknowledged that the specification describes and enables amino acid sequences that are at least 70% identical to SEQ ID NOs:5 or 6 (and which have the recited function of FGF-2), and therefore, Applicants submit that the claims, as amended, meet the requirements of 35 U.S.C. § 112, first paragraph.

In view of the foregoing discussion, Applicants respectfully request that the Examiner withdraw the rejection of Claims 1-3, 6, 8, 10-18 and 43-46 under 35 U.S.C. § 112, first paragraph.

Rejection of Claim 12 Under 35 U.S.C. § 112, Second Paragraph:

The Examiner has rejected Claim 12 under 35 U.S.C. § 112, second paragraph, on the basis that the phrase "58 through 43" is not in numerical order and renders the claim confusing.

Since this appears to be a duplicate of the prior phrase, which is presented in numerical order, Applicants have amended Claim 12 to remove the phrase found objectionable by the Examiner. In

view of the foregoing amendment and remark, Applicants respectfully request that the Examiner withdraw the rejection of Claim 12 under 35 U.S.C. § 112, second paragraph.

Double Patenting Rejection

The Examiner has advised that if Claim 16 is found to be allowable, then Claim 17 will be rejected as being a substantial duplicate, since both claim the same protein.

To expedite prosecution, Applicants have cancelled Claim 17, without prejudice to or disclaimer of the subject matter therein.

Applicants have attempted to address all of the Examiner's concerns as set forth in the November 17 Office Action. It is believed that the claims are in a condition for allowance and therefore, if the Examiner has any remaining issues, she is respectfully requested to contact the below-named agent at (303) 863-9700 to expedite the resolution of prosecution.

Respectfully submitted,

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